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II. "Contributions to the Physiology of the Liver—Influence of Alkalies." By FREDERICK W. PAVY, M.D. Communicated by Dr. SHARPEY, Sec. R.S. Received January 24, 1861.

I have already communicated to the Royal Society the fact that the introduction of an alkali, as the carbonate of soda, into the circulation, prevents the production of diabetes in an animal after an operation on the sympathetic nerve that otherwise occasions it. On excising, for example, the superior cervical ganglia, or dividing the ascending branches of the superior thoracic ganglia, diabetes is an almost constant result in the dog. Now, I have a record of ten experiments, in which, before attacking the superior cervical ganglia, 200 grains, or nearly so, of the crystallized carbonate of soda dissolved in a small quantity of water, were introduced into the general circulation through the jugular vein. In not one of these cases was there any diabetes produced. In another instance, where I employed only 100 grains of the carbonate of soda, the urine soon after the operation on the ganglia became decidedly, although not strongly saccharine. On dividing the ascending branches of the superior thoracic ganglia also, after the introduction of 200 grains of carbonate of soda, I have failed to meet with sugar in the urine. Under this injection of 200 grains of carbonate of soda into the circulation, the urine becomes exceedingly copious in quantity, pale-coloured, and alkaline to test-paper, and effervesces strongly on the addition of an acid.

Although the introduction of carbonate of soda into the system thus counteracts the influence of certain lesions of the sympathetic in leading to the production of sugar (I presume) in the liver, yet it is not sufficient to prevent the appearance of sugar in the urine where life has been destroyed and the circulation is kept up artificially. On resorting to artificial respiration immediately after death, the action of the heart being kept up, the sugar which is formed in the liver, as the result of a *post-mortem* occurrence, escapes from it into the blood, and in passing through the kidneys is eliminated by these organs. In two experiments I introduced 200 grains of carbonate of soda into the jugular vein previous to the destruction of life by

pithing. The circulation was maintained by artificial respiration; an enormous flow of alkaline urine took place, which in both cases presented a saccharine character.

From another experiment, however, it is evident that the carbonate of soda, if it arrives at the liver in sufficient quantity, holds in check the tendency of hepatine to pass into sugar, and thus prevents the production of saccharine urine when the circulation is kept up artificially after death. Introduced into the general venous system, as in the two experiments mentioned, the amount of the carbonated alkali that reached the liver was insufficient to counteract the ordinary *post-mortem* change. Introduced into a branch of the portal system, it must all pass to the liver, and accordingly the result is altered. I injected 200 grains of carbonate of soda, dissolved in an ounce of water, into a branch of the portal vein of a dog. The animal was killed by destroying the medulla oblongata. Artificial respiration was performed for an hour and three quarters, during the whole of which time the heart continued beating vigorously. The urine contained in the bladder at the end of the experiment was pale-coloured and alkaline, and effervesced slightly on the addition of an acid. It did not give evidence of even a trace of sugar. The blood which escaped on opening the body behaved precisely as it does under natural circumstances, and gave just a trace of reaction with the copper solution. The liver, examined a short time after removal, was quite devoid of sugar. The presence of hepatine, however, was easily recognized, and in the course of twenty-four hours sugar had been produced, so as to give a copious orange-red reduction with the copper solution.

Looking to these facts, I determined to investigate the effects of an alkali on the hepatine in the liver during life. I had long since noticed that the carbonate of potash introduced into the stomach caused a disappearance of hepatine in a short space of time without the production of sugar. I had injected 200 grains dissolved in two ounces of water, through the œsophagus into the stomach of a dog that had recently been fed. An examination of the blood before and at intervals after the injection, gave no sign of any difference being produced. The animal died during the night; and from its condition in the morning it was probable that death had taken place within twelve hours after the injection. The liver was much altered

from its natural appearance, and did not contain a trace of either hepatine or sugar.

In other experiments, where carbonate of soda was introduced into the stomach and duodenum, I found that when the animal had lived several hours, the hepatine had entirely disappeared; but when it was killed within three or four hours, some amount of hepatine remained.

Absorption having had to take place, the passage of the carbonated alkali to the liver can only have been comparatively gradual. On the other hand, the rapid distribution of it in tolerable quantity through the organ, as by injecting it into a branch of the portal vein, causes a transformation of hepatine into something else than sugar in an astonishingly short period of time. I regard the discovery of this fact as a most important step in our study of the physiological history of hepatine, and believe that it is not unlikely to lead us to a knowledge of its natural destination in the economy.

In proof of the effect produced by the injection of a solution of carbonate of soda into the portal system during life, I will give the leading features of the first three experiments that I performed.

In the first, sixty grains of carbonate of soda dissolved in five drachms of water were injected into one of the mesenteric veins of a healthy, nearly full-grown pup. Between one and a half and two hours afterwards the animal was killed by pithing. The liver was much swollen, dark-coloured from congestion, and easily lacerable. The walls of the gall-bladder were thickened from œdema, and the tissue in the neighbourhood of the transverse fissure of the liver was also quite œdematous. The liver contained neither hepatine nor sugar. The blood collected from the right side of the heart was also quite free from sugar.

In the second experiment, fifty grains of the carbonate, dissolved in four drachms of water, were employed as the injection. In performing the operation, the stomach was observed to contain food, and the lacteals to be well injected with chyle. Four hours afterwards the dog was pithed. The liver was devoid of both hepatine and sugar. The blood from the right side of the heart was likewise devoid of sugar. The urine found in the bladder presented an alkaline reaction, and effervesced slightly on the addition of an acid; like the liver and blood, it was quite devoid of sugar. In the third,

80 grains, dissolved in 6½ drachms of water, constituted the injection used. In one hour's time the dog was killed. The liver was dark-coloured and exceedingly congested, fluid blood oozing out of it in large quantity when it was sliced. Neither hepatine nor sugar was present.

Here, then, were the experiments which taught me that, under the influence of the presence of a certain quantity of carbonate of soda, the whole of the hepatine in the liver might be destroyed in a short space of time during life, without any appearance of the production of sugar. The animals submitted to these experiments were perfectly good-conditioned and healthy, and under such circumstances hepatine is always found to some considerable extent in the liver. There could not be the slightest doubt that hepatine would have been met with had not the carbonate of soda exercised a special action in promoting its rapid disappearance or transformation. In one of the experiments, it will be observed that this had been entirely effected in an hour.

From many subsequent experiments I learnt that, to obtain the result I have mentioned, certain circumstances require to be attended to in making the injection. In some experiments I did not meet with a similar total disappearance of hepatine, although even a larger quantity of carbonate of soda had been employed. I subsequently found that this depended on the circumstance that, when the injection is made slowly, and the blood is flowing freely through the system, the carbonate of soda passes in great part through the liver without effecting a total disappearance of its hepatine or materially altering its natural aspect; whereas, when the carbonated alkali is rapidly thrown in, it seems to cause an obstruction to the flow of blood through the organ, and to exude into, and thus be detained in its tissue. This may be seen on watching the liver whilst the injection is being effected; a number of small light-coloured spots, constituting the lobules influenced by the injection, first make their appearance, and the liver rapidly becomes dark-coloured, swollen, and turgid with blood. It may still, however, allow the blood to move through it; but in some cases, in which I have used a large quantity of the carbonate in a concentrated state, 200 grains for instance in an ounce of water, the circulation through the liver has evidently become stopped, for the chylo-poietic viscera have presented exactly the appearance

as if the portal vein had been obstructed by ligature or otherwise. Holding the muzzle of the animal so as temporarily to check its breathing, and so impede the escape of blood from the liver during the introduction of the solution, has the same effect as injecting it rapidly. The carbonate of soda is delayed in the liver so as to bring about the chemical and physical alteration I have noticed.

If, then, the conditions of the experiment are such as to conduce to the free passage of the injected solution through the liver, the hepatine escapes the influence requisite to cause its rapid and complete disappearance. But, should the circumstances be favourable to the saturation of the parenchyma of the liver with the carbonated alkali, the hepatine is so rapidly transformed that it soon ceases to be discoverable.

In the experiments mentioned, the hepatine completely disappeared in the space of an hour; a much shorter time, however, than this is required; for I have found that even within a few minutes of the injection being completed the liver has been totally deprived of hepatine. Thus, in one experiment, 200 grains of carbonate of soda in one ounce of water were injected into a branch of the portal vein of a good-sized, good-conditioned dog that had been fed about twenty hours previously; as soon as the vein was ligatured, the animal being kept under the influence of chloroform, one of the lobes of the liver was tied at its base and removed; examined within a very short time afterwards, it was found perfectly free from both hepatine and sugar. In another experiment, 100 grains of carbonate of soda in half an ounce of water were injected into one of the mesenteric veins of a large, exceedingly good-conditioned dog that had been likewise fed about twenty hours previously. When the injection was completed, a portion of the liver was obtained and examined; it was quite devoid of hepatine, but contained just a discoverable trace of sugar; this probably existed in the liver before the injection, and was formed in consequence of the congestion to which the organ was purposely submitted by temporarily obstructing the breathing.

I have tried the substitution of the caustic for the carbonated alkali, but there are accidental circumstances occasioned by its use which render it unfit for employment. Fifty grains of caustic potash were dissolved in one ounce of water and introduced into a branch of the portal vein. After the injection was completed and the vein

secured, hæmorrhage of dark pitchy blood took place from a vessel which gave way through the action of the alkali upon it. This was very soon checked, and the animal lived, although in a comatose state, for about an hour. Upon examining the liver after death, it was found that it had not been uniformly penetrated by the alkali, and that the large veins were plugged up with coagulated or solidified blood, which had arrested the portal circulation; I have never observed a similar solidification of the blood produced by the use of the carbonate of soda. My analysis of the liver a short time after death indicated the presence of both hepatine and sugar. It was quite evident from the appearance of the organ, that much of its tissue had not been reached by the injection, and therefore escaped the action of the alkali.

It having been thus shown that a rapid disappearance of hepatine may be occasioned by the presence of the carbonate of soda in the liver during life, it remains now to determine the nature of the process of disappearance, and to discover the material into which the hepatine is transformed. I am not in a position as yet to enter satisfactorily into a discussion of this question; but, if I cannot state how and into what the hepatine is thus changed—if I cannot at present speak definitely upon the positive side of the question, I, however, can advert to its negative aspect, and say what the process is not; and, in following this course, I am adopting a rational proceeding, for it is from a consideration of the known that we are placed in the best position for making a profitable advance towards the unknown.

As hepatine is a body presenting such characteristic reactions, and so easily susceptible of recognition, we can have no difficulty in deciding that it is really absent or transformed in the circumstances stated, and that it is not merely masked or concealed by the material employed for injection. It is the property of hepatine to be thrown down as a white precipitate by spirit. The alkalies and carbonated alkalies, for certain, do not prevent this precipitation from taking place. A solution of hepatine presents a most striking lactescence; and by this character, used with precaution, not only may the question of its presence or absence be decided, but, when present, its relative amount may be pretty accurately judged of in different specimens. With iodine it gives a strong deep-red coloration. Lastly,

boiled with a little sulphuric acid, or treated when in a neutral state with saliva, at a moderately elevated temperature, it undergoes transformation into sugar. Now it is not upon the evidence of one, but of all these tests, that I have relied.

Does the hepatine disappear by being metamorphosed into sugar? If so, taking an ordinary sized liver, say $7\frac{1}{2}$ ounces in weight, containing an average amount of hepatine for an animal diet, say seven per cent.; and reckoning (in accordance with my analyses showing the relation of loss of hepatine to gain of sugar in the liver after death) that the loss of one and a half part of the former is accompanied with the production of one part of the latter, then upwards of 150 grains of sugar have to be accounted for. Under such circumstances sugar ought to be easily detected in quantity in the liver and blood; or else it must be assumed to be decomposed as fast as it is formed. But, as I have mentioned, the liver in my experiments has been found free from sugar as well as hepatine, and the blood has exhibited a similar state, or has only been charged to a slight extent—a condition that has probably existed previous to the injection, and been produced by the preliminary part of the experiment, chloroform having been always used to occasion anæsthesia. The sugar, then, is not to be discovered, and we shall find the other hypothesis to be equally untenable.

When sugar is present either in the liver or blood, I have failed to discover that the introduction of a carbonated alkali exercises any perceptible influence over it. It is true that, in order to avoid error, certain precautions are necessary in preparing a liquid from an alkaline specimen for the application of the copper test. If the decoction of the liver is allowed to remain only in a slight degree alkaline, a certain amount of albuminous matter is retained in solution, which interferes materially with the action of the test. If acetic acid be used to neutralize, a small excess of this will produce the condition that it was intended to avoid. I find, however, that citric acid is not liable to this objection; and, accordingly, if it be added in slight excess to a specimen of alkaline liver, a decoction can be prepared in which the slightest amount of sugar or of hepatine may be easily and certainly recognized.

To show that when sugar is formed the carbonate of soda has no power of destroying it, I may refer to the following experiment, which

accords with my general experience. Into the liver of a small dog, about ten minutes after the destruction of its life, 100 grains of carbonate of soda in half an ounce of water were injected through the portal vein; in a couple of hours an examination was made; the decoction of liver, prepared as I have recommended, gave the usual orange-red reduction with the copper-solution that is observed where the *post-mortem* change has been allowed to take place. Should hepatine in fact be transformed into sugar, the latter will unquestionably be discoverable, notwithstanding the presence of an alkali or alkaline carbonate.

I have tried the effect of injecting grape-sugar along with carbonate of soda into the liver during life, and the result was in strict accordance with what I have just stated. 200 grains of each were dissolved together in an ounce of water, and injected into one of the mesenteric veins of a good-sized healthy dog; some blood taken from the carotid artery after the operation was found to be charged with sugar to a large extent. In one hour's time the animal was killed. The liver and blood were both found saccharine. The urine contained in the bladder was mixed with blood, which I have observed always to be the case when such an amount as 200 grains of the carbonate of soda has been employed. After being boiled and filtered, it was tested with the copper solution, and gave a strong reaction of the presence of sugar.

The evidence before us tends, I think, satisfactorily to prove that the hepatine is neither concealed nor transformed into sugar when lost sight of after injection of the carbonate of soda. Again, it does not seem that its disappearance can be owing to any direct chemical action of the carbonated alkali. It is one of the most striking properties of hepatine to resist the action of even the caustic alkali at a boiling temperature, and I certainly have not been able to perceive that the carbonated alkali is capable of exercising any direct chemical influence upon it up to a boiling heat.

Looking to all the facts in my possession, I am inclined to believe, although I cannot at present substantiate the opinion, that the rapid disappearance of hepatine which has been noticed, is due to one of those catalytic actions of which we have such numerous examples occurring amongst the phenomena of life. It is well known that sugar, under the influence of certain catalytic conditions, is transformed

into alcohol and carbonic acid, and under others into lactic acid. Now, may not hepatine occupy a parallel position, and be susceptible of undergoing a process of metamorphosis besides that into sugar, the product having as yet escaped discovery? Hepatine itself is a body that has been known to us but a very short period.

I have mentioned that the carbonate of soda does not enjoy any direct chemical power of effecting a destruction of hepatine up to the temperature of ebullition; neither, as far as I have yet learnt, can it occasion a disappearance of it from the liver after death: it, however, holds the saccharine metamorphosis in check. Previous to this inquiry, although I had known that a tolerably strong solution of the caustic alkali prevented the production of sugar in the liver after death, I was not aware that a moderate amount of the carbonated alkali has so completely the same effect. In an experiment recently performed, I injected, instantly after the animal was pithed, 200 grains of the carbonate of soda dissolved in an ounce of water, into the liver through the portal vein: a couple of lobes happened to escape being properly penetrated by the injection, and in this part of the liver the ordinary *post-mortem* production of sugar took place. In the other portion of the organ no saccharine metamorphosis occurred; nor could I discover that the injection had in any degree caused a disappearance of the hepatine, as happens under its operation during life. The liver examined shortly after the introduction of the carbonate of soda had been completed, was found to be highly charged with hepatine and quite devoid of sugar; examined again on the following day, the result was identically the same.

Amongst my examinations of the livers of the lower animals, I once met with a specimen from a cod-fish in which the hepatine resisted the ordinary *post-mortem* transformation into sugar. Hepatine was present in the greatest abundance, but there was only the merest trace of sugar discoverable when first examined, and likewise after it had been standing aside for twenty-four hours. It was then exposed to a moderately elevated temperature for three hours, and still indicated only a trace of the presence of sugar, notwithstanding that the decoction immediately produced sugar copiously on being treated with saliva. The result being so much at variance with that usually met with, made a strong impression upon me. I can only see two ways of accounting for it; either the hepatine was protected

from the influence of catalytic action in some such manner as in my experiment with the injection of carbonate of soda into the liver instantly after death, or the absence of change depended upon a want of the requisite catalytic agent.

I cannot help regarding it as a most significant fact, which, however, I merely mention here, without at present commenting upon it, that after the introduction of carbonate of soda into the system, the liver gives upon analysis so high a per-centage of fat. The usual quantity of fat in the liver of the healthy dog kept upon an animal diet, I have found to be about six per cent. It is seldom much more, and often only three or four per cent. After the introduction of carbonate of soda into the system, my analyses have given me from ten to twelve and thirteen, and even more than this per cent. The employment of large quantities of the carbonate does not seem to have the effect I have just mentioned. It is only where the liver is injected with a moderate amount that the high per-centage of fat is noticeable: I do not think that the hepatine is directly transformed into fat, but there is, I have strong reason to believe, a close connexion between the two; at all events, it is a point that I have grounds for endeavouring to work out. The formation of the bile also, from what I have observed, appears to be involved in this question, and forms a subject of consideration in the investigation I am conducting.

The conclusions advanced in this communication are:—

"That the introduction of carbonate of soda into the circulation prevents the production of saccharine urine after lesions of the sympathetic nerve otherwise occasioning it.

"That carbonate of soda injected into the general venous system does not prevent the urine from becoming saccharine after the destruction of life when the circulation is kept up artificially; but injected into the portal system, so that all may pass into the liver, it has the effect of keeping the urine entirely free from sugar.

"That carbonate of soda injected into the portal system during life, causes a rapid disappearance of hepatine from the liver without any sign of the production of sugar.

"That in the disappearance of hepatine under the influence of the carbonate of soda, the hepatine is not concealed, nor transformed into sugar, nor destroyed by any direct chemical power possessed by the carbonated alkali. The facts before me would suggest that it is

transformed by a process of the nature of catalysis, the product having as yet escaped discovery.

"That carbonate of soda injected into the liver after death does not effect a disappearance of hepatine, but even in moderate quantity holds the saccharine metamorphosis completely in check.

"That there is probably a close connexion between the disappearance of hepatine, the production of fat, and the state of the bile."

February 7, 1861.

Major-General SABINE, R.A., Treasurer and Vice-President, in the Chair.

The Right Hon. the Earl of Ellesmere and Professor Harkness were admitted into the Society.

The BAKERIAN LECTURE was then delivered by Professor TYNDALL, F.R.S., "On the Absorption and Radiation of Heat by Gases and Vapours, and on the Physical Connexion of Radiation, Absorption, and Conduction."

The Lecturer gave an account of the researches which form the subject of a paper with the above title, communicated by him to the Society; and in explaining the methods followed, he exhibited the apparatus which he had employed in his experiments. The following is an abstract:—

(Abstract.)

The apparatus made use of in this investigation consists of the following parts:—

1. A copper cube C, containing water kept constantly boiling, and one of whose faces, coated with lampblack, forms the source of radiant heat.

2. A brass tube 2·4 inches in diameter, which is divided into two portions, α and β.

α. The portion of the tube intended to receive the gases and vapours; it is stopped air-tight at its two ends by plates of transparent rock-salt, and is attached to a good air-pump, by which it can be exhausted at pleasure. The length is 4 feet.